Oncology Clinical Pathways
Prostate Cancer

July 2023 – V4.2023

Table of Contents

Prostate Cancer – Presumptive Conditions

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Vietnam Veterans – Agent Orange Exposure or Specified Locations

- Prostate cancer

Gulf War and Post 9/11 Veterans

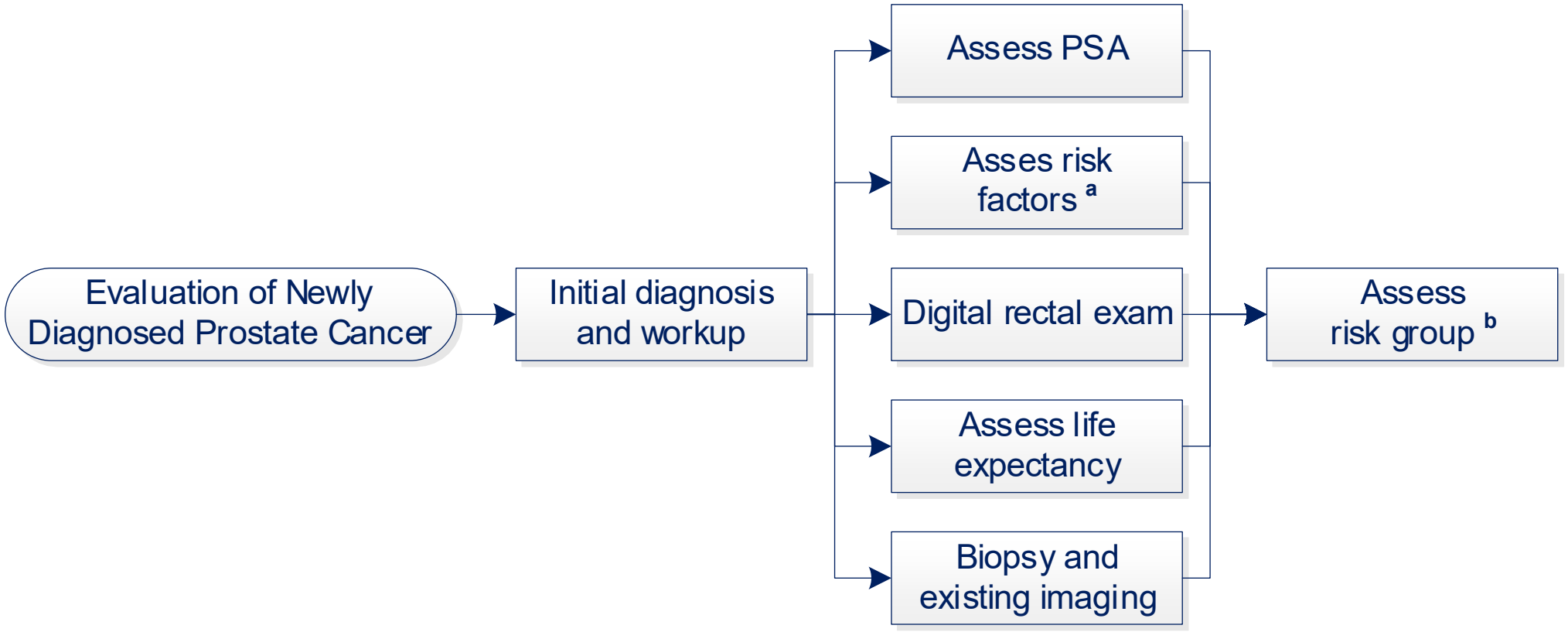
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Reproductive cancers of any type

* The Southwest Asia theater of operations refers to Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, and the airspace above these locations.

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov)

Prostate Cancer – Evaluation of Newly Diagnosed



Clinical trial(s) always considered on pathway.

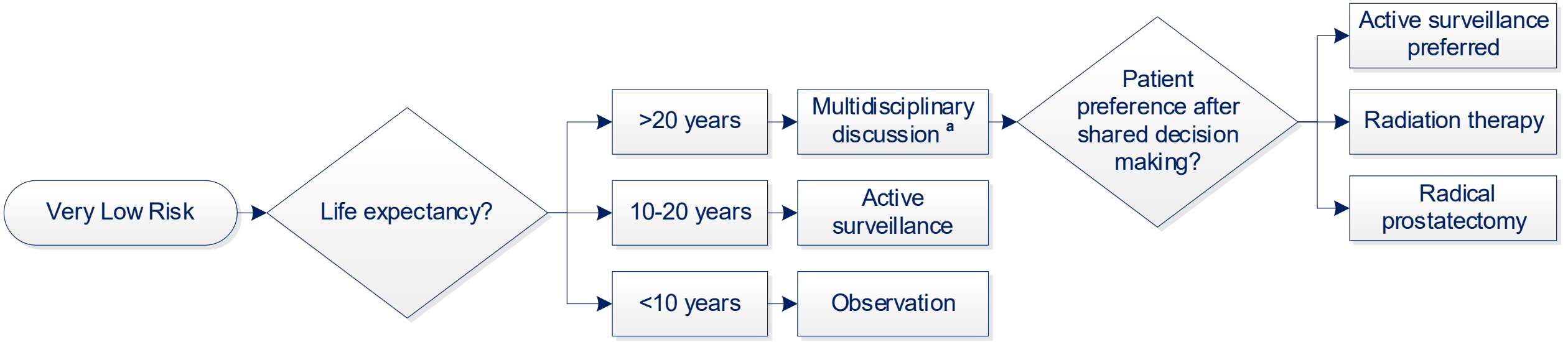
[a] **Risk Factors** Race, Agent Orange exposure, family history, known germline mutation

[b] **Risk Groups** Refer to risk stratification and corresponding pathways

Prostate Cancer – Risk Stratification

Risk Group	Defined by Clinical/ Pathologic Features			Imaging for Nodal or Metastatic Disease	Germline Testing	Initial Therapy
Very low	All the following: • T1c • Grade group 1 • PSA < 10 ng/ml • < 3 prostate biopsy fragments/ cores positive; ≤ 50% cancer in each fragment/core • PSA density < 0.15 ng/ml/g			Not indicated	Recommended for any of the following: • Ashkenazi Jewish ancestry • Family history of high-risk germline mutations • Strong family history of cancer	Follow **Very Low Risk** pathway
Low	All the following: • T1-T2a • Grade Group 1 • PSA < 10 ng/ml					Follow **Low Risk** pathway
Intermediate	All the following: • No high-risk group features • No very high-risk group features • One or more intermediate risk factors (IRF) ○ T2b-T2c ○ Grade Group 2 or 3 ○ PSA 10-20 ng/ml	***Favorable Intermediate***	All the following: • One IRF • Grade Group 1 or 2 • < 50% positive biopsy cores	• Bone imaging not recommended for staging • Pelvic ± abdominal imaging recommended if nomogram predicts >10% probability of pelvic LN involvement		Follow **Favorable Intermediate Risk** pathway
		Unfavorable Intermediate	At least one of the following: • 2 or 3 IRFs • Grade Group 3 • ≥ 50% positive biopsy cores	• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings • Consider molecular imaging if available		Follow **Unfavorable Intermediate Risk** pathway
High	At least one high-risk feature: • T3a • Grade Group 4 or 5 • PSA > 20 ng/ml			• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings • Consider molecular imaging if available	Recommended	Follow **High or Very High-Risk** pathway
Very High	At least one of the following: • T3b-T4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • > 4 cores with Grade Group 4 or 5			• Bone and Soft Tissue Imaging: use PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings • Consider molecular imaging if available	Recommended	
Regional	Any T, N1, M0: Consider testing tumor for HRRm and MSI or dMMR				Recommended	Follow **Regional Risk** pathway
Metastatic	Any T, Any N, M1: Recommend testing tumor for HRRm and MSI or dMMR				Recommended	Follow **CSPC M1** pathway

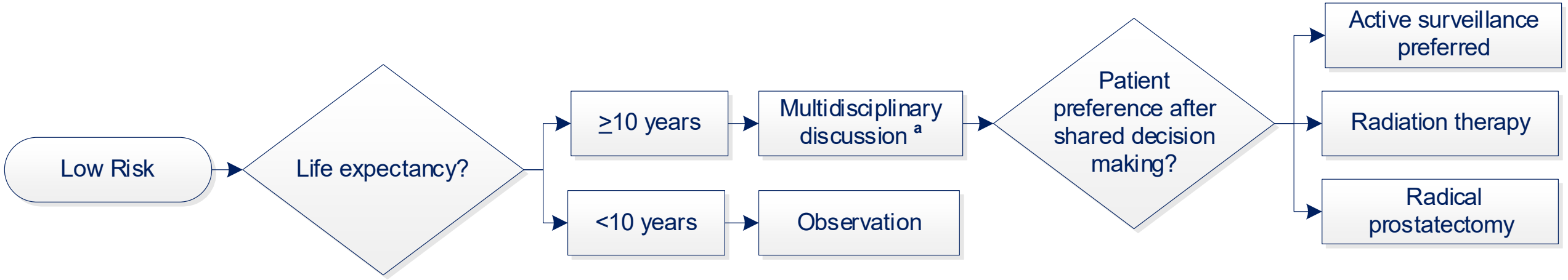
Prostate Cancer – Very Low Risk Group



Clinical trial(s) always considered on pathway.

[a] **Multidisciplinary Discussion** to include Radiation Oncology, Urology

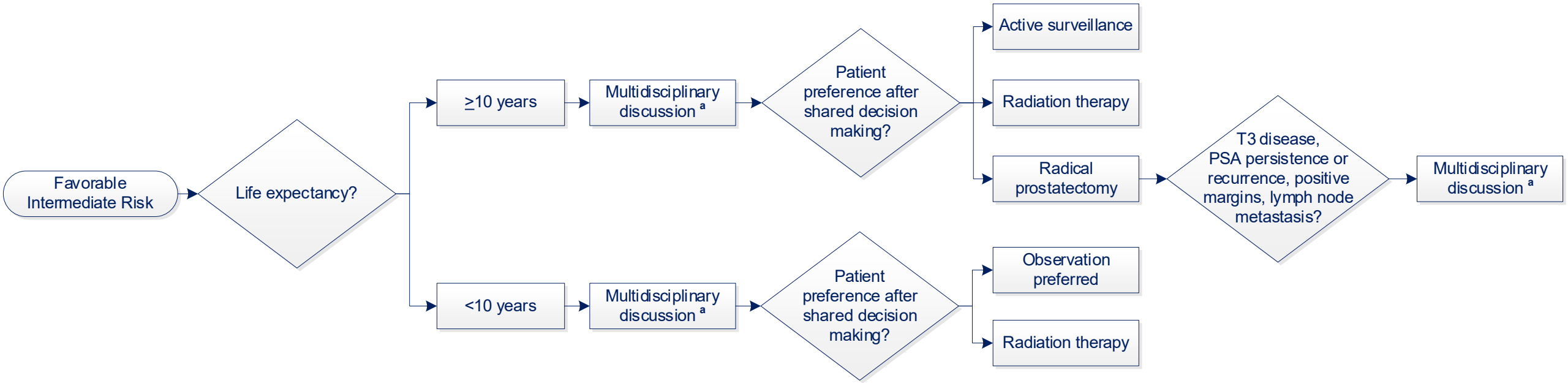
Prostate Cancer – Low Risk Group



Clinical trial(s) always considered on pathway.

[a] **Multidisciplinary Discussion** to include Radiation Oncology, Urology

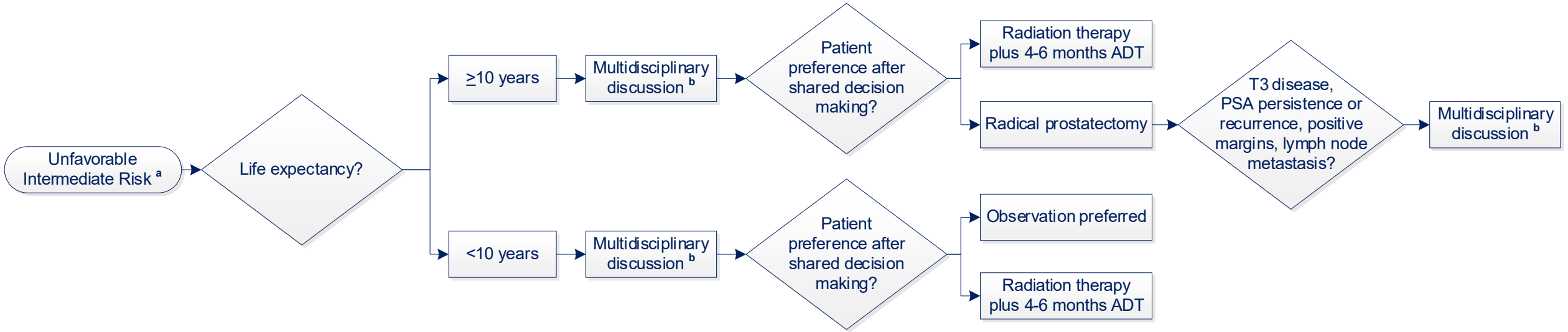
Prostate Cancer – Favorable Intermediate Risk Group



Clinical trial(s) always considered on pathway.

[a] **Multidisciplinary discussion** to include Radiation Oncology, Urology

Prostate Cancer – Unfavorable Intermediate Risk Group

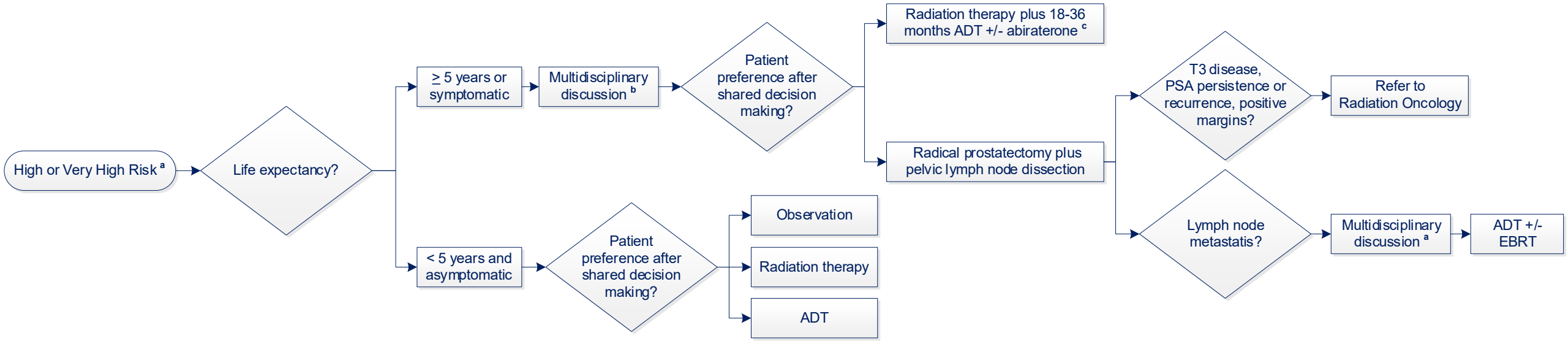


Clinical trial(s) always considered on pathway.

[a] **Imaging** PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings

[b] **Multidisciplinary Discussion** to include Radiation Oncology, Urology, Medical Oncology

Prostate Cancer – High or Very High Risk Group



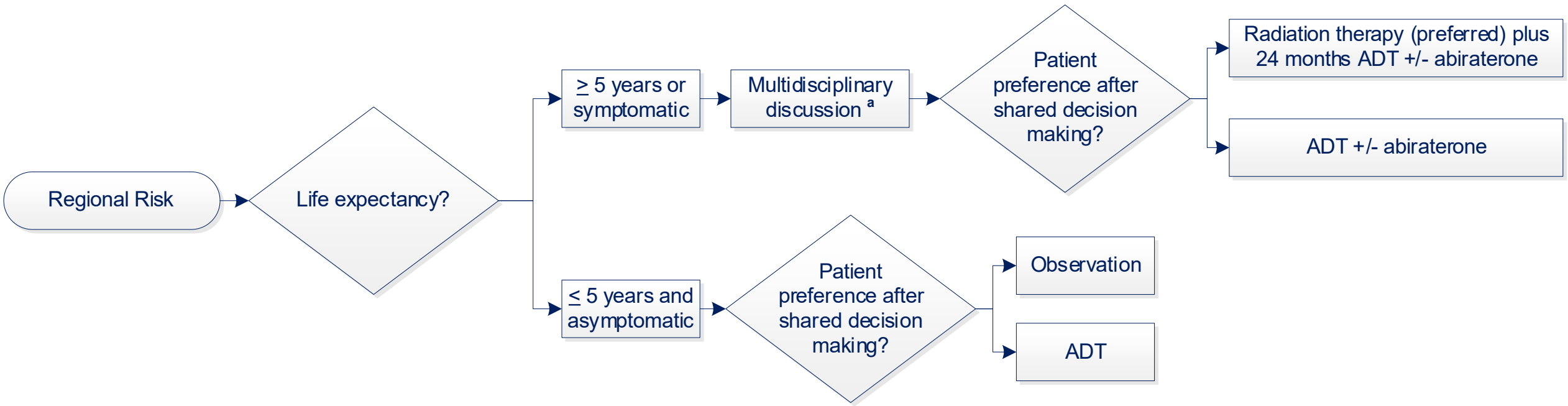
Clinical trial(s) always considered on pathway.

[a] **Imaging** PSMA PET/CT, (or PET/MRI) if available, or a combination of bone imaging (with either Tc99m-MDP/HDP SPECT/CT, F18-NAF PET/CT) + soft tissue imaging (with CT, MRI, F18-fluciclovine PET) + PSMA PET/CT for equivocal findings

[b] **Multidisciplinary Discussion** to include Radiation Oncology, Urology, Medical Oncology

[c] **Abiraterone** prescribe only for very high risk group patients; duration for maximum of 2 years

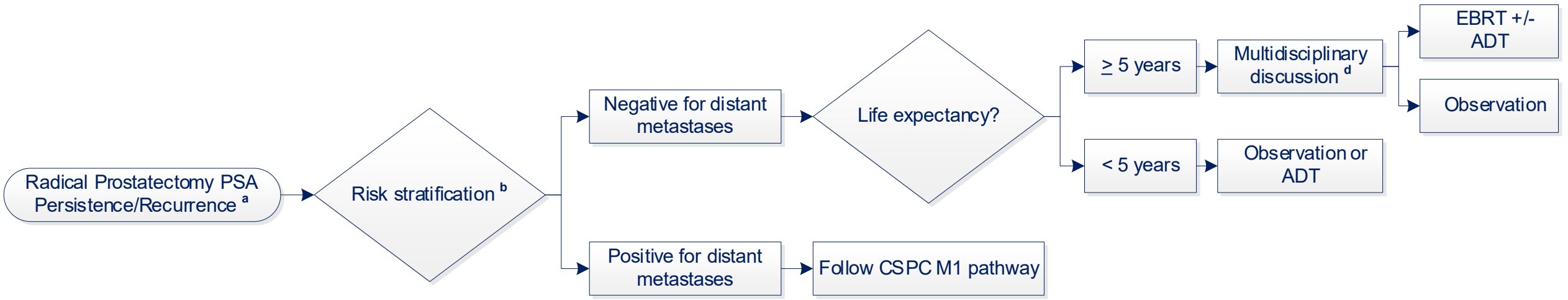
Prostate Cancer – Regional Risk Group



Clinical trial(s) always considered on pathway.

[a] **Multidisciplinary Discussion** to include Radiation Oncology, Urology, Medical Oncology

Prostate Cancer – Radical Prostatectomy PSA Persistence/Recurrence



Clinical trial(s) always considered on pathway.

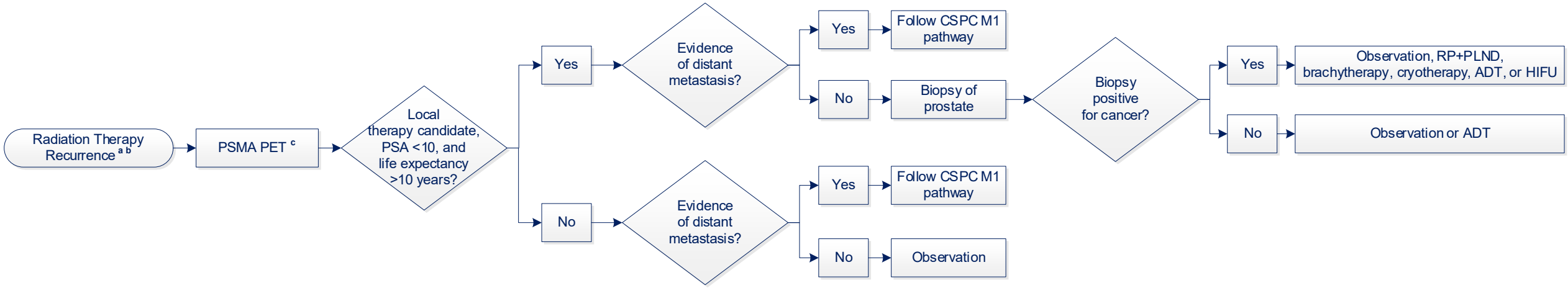
[a] **PSA Persistence/Recurrence** defined as rising, detectable PSA based on at least two determinations

[b] **Risk Stratification** PSADT; pathology report: PSMA PET imaging, if not available: fluciclovine PET/CT; CT chest/abdomen/pelvis; bone imaging with Tc99m-MDP/HDP SPECT/CT or F18 sodium fluoride PET/CT (or PET/MRI); MRI prostate/pelvis; provider appropriateness review and consideration should be made for imaging evaluation in the setting of early recurrence with low PSA values (<0.5 ng/ml)

[c] **Multidisciplinary Discussion** to include Radiation Oncology, Urology, Medical Oncology

EBRT External Beam Radiation Therapy

Prostate Cancer – Radiation Therapy Recurrence



Clinical trial(s) always considered on pathway.

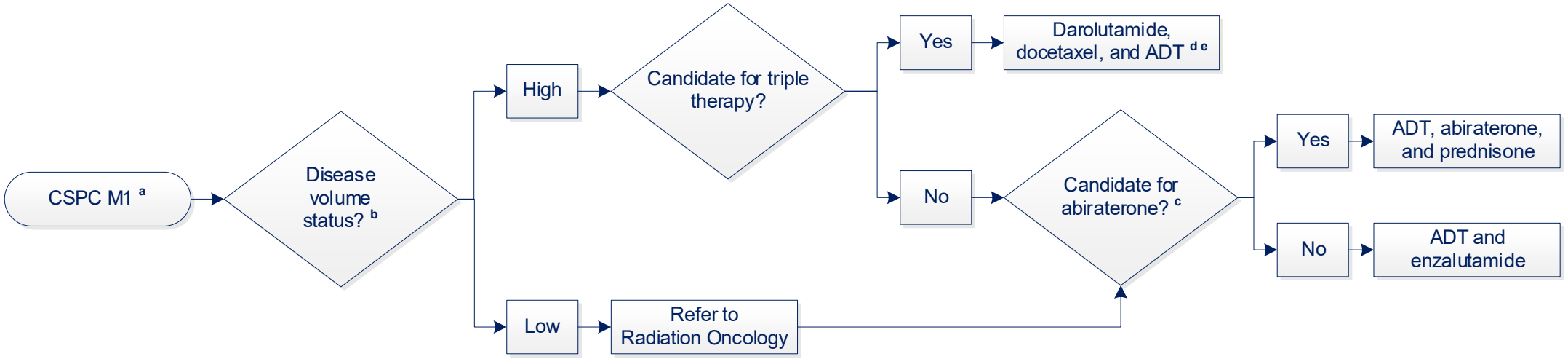
[a] **Recurrence** defined as rising PSA >2 above Nadir or positive DRE post-curative intent radiation

[b] **PSA Bounce** defined as a transient rise in PSA, at a median of 12-18 months after treatment; PSA bounce may occur in the absence of recurrent disease and does not necessarily signify a treatment failure or constitute an indication for intervention

[c] **PSMA PET** if not available, recommend prostate MRI and fluciclovine PET/CT or CT chest/abdomen/pelvis and bone imaging (technetium bone scan or F-18 sodium fluoride PET)

RP Radical Prostatectomy
PLND Pelvic Lymph Node Dissection
HIFU High Intensity Focused Ultrasound

Prostate Cancer – Castrate Sensitive Prostate Cancer (CSPC) M1



Clinical trial(s) always considered on pathway.

[a] **First Generation Antiandrogens** not recommended for long-term use however short course may be administered to block testosterone flare

[b] **Low-volume disease** defined as no visceral metastases and four or less bone metastases; **high volume disease** is differentiated from low-volume disease by visceral metastases and/or more than four bone metastases

[c] **Abiraterone** contraindications include hepatic dysfunction [f], significant cardiovascular disease [g], uncontrolled hypertension, or the inability to tolerate prednisone

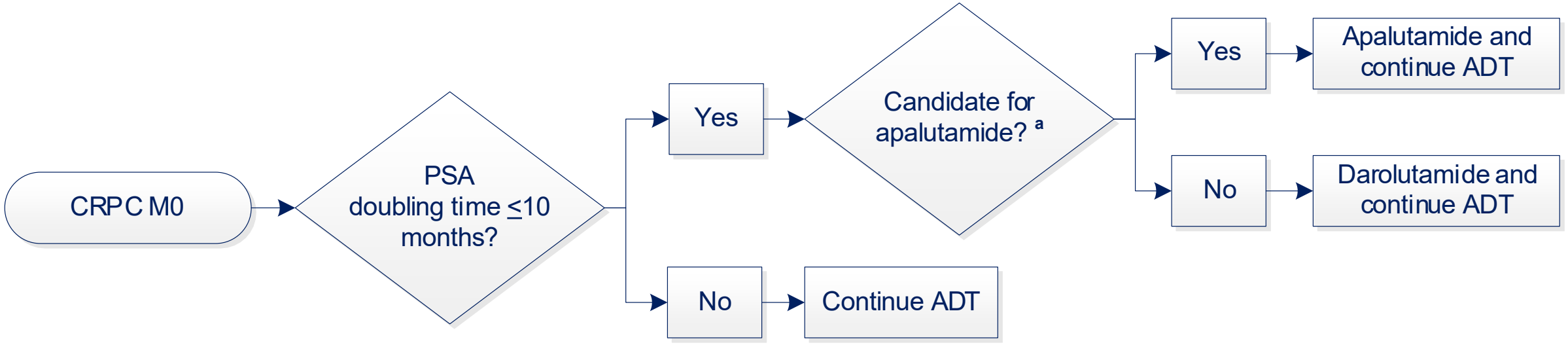
[d] **Inclusion Criteria** includes ECOG 0-1 and distant metastasis (M1) detected on imaging

[e] **Exclusion Criteria** includes CVA, MI, unstable angina, CHF (NYHA class III or IV) in the prior 6 months and/or uncontrolled HTN

[f] **Hepatic Dysfunction** defined as baseline Tbili ≥ 1.5 x ULN (except in Gilbert's Disease), AST or ALT ≥ 2.5 x ULN (AST or ALT ≤ 5x ULN allowed in known liver metastases), and/or Child-Pugh Class C

[g] **Significant CV disease** defined as MI or ATE in past 6 months, severe or unstable angina, NYHA Class III or IV heart failure, and/or EF < 50% at baseline

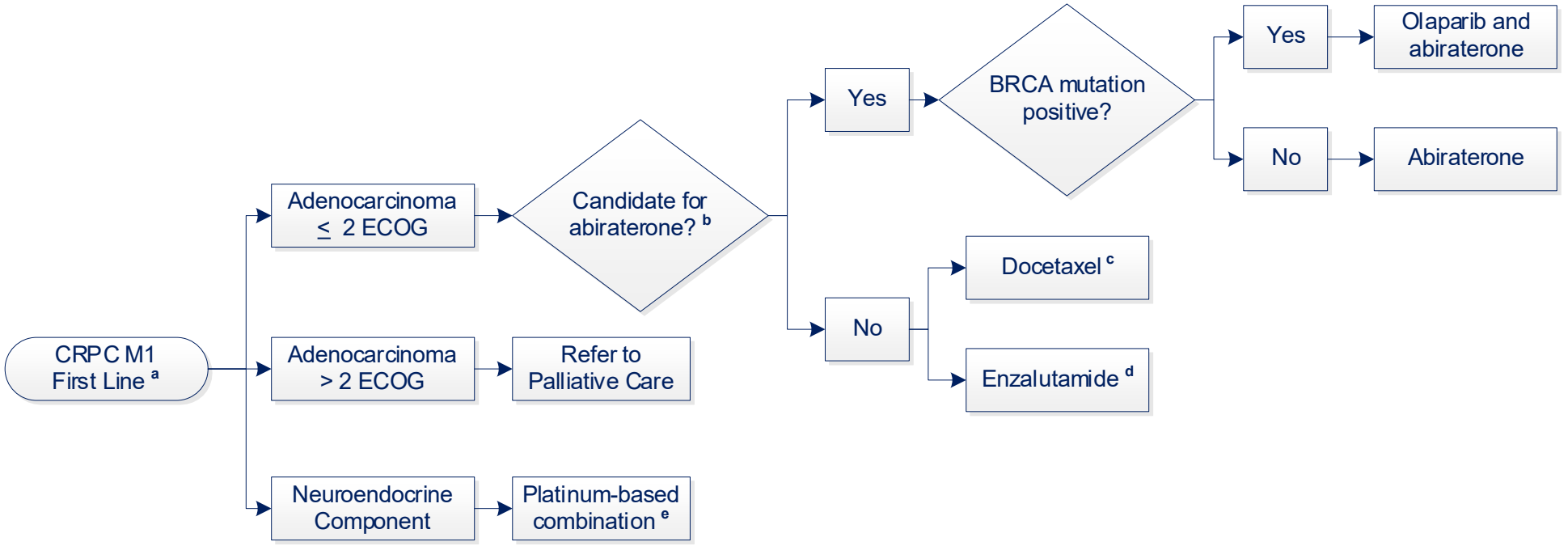
Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M0



Clinical trial(s) always considered on pathway.

[a] **Apalutamide** contraindications include history of severe renal or hepatic dysfunction, cardiovascular or cerebrovascular event in prior 6 months, high fall risk, or seizure history

Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M1, First Line



Clinical trial(s) always considered on pathway.

[a] **Consider Biopsy** in setting of visceral disease or atypical progression (scan worsening without overt PSA progression); continuous ADT with testosterone goal <50

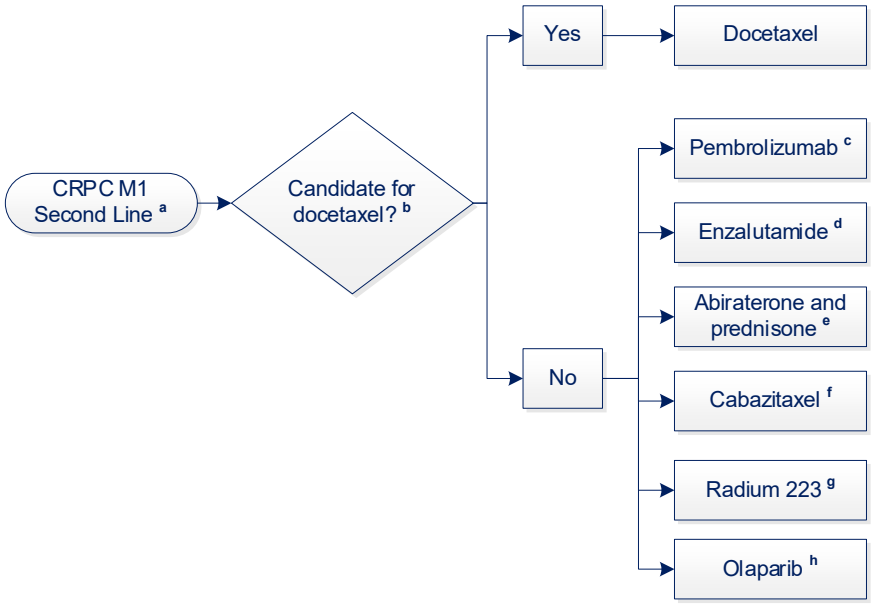
[b] **Abiraterone** contraindications include hepatic dysfunction, significant cardiovascular disease, uncontrolled hypertension, or the inability to tolerate prednisone

[c] **Docetaxel** prescribe for relatively rapidly progressing symptomatic disease

[d] **Enzalutamide** contraindications include severe renal impairment (CcCl <30 ml/min), seizure history, and/or brain metastases/active epidural disease

[e] **Platinum-Based Combination** No regimen proven more effective than another

Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M1, Second Line



Clinical trial(s) always considered on pathway.

[a] **Consider Biopsy** in setting of visceral disease or atypical progression (scan worsening without overt PSA progression); continuous ADT with testosterone goal <50

[b] **Docetaxel** prescribe for relatively rapidly progressing symptomatic disease

[c] **Pembrolizumab** prescribe if patient has MSI-H (microsatellite instability-high), dMMR (deficient mismatch repair) or TMB high in tumor agnostic fashion

[d] **Enzalutamide** prescribe if not previously received (response unlikely if previously progressed on abiraterone); contraindications include severe renal impairment (CcCl <30 ml/min), seizure history, and/or brain metastases/active epidural disease

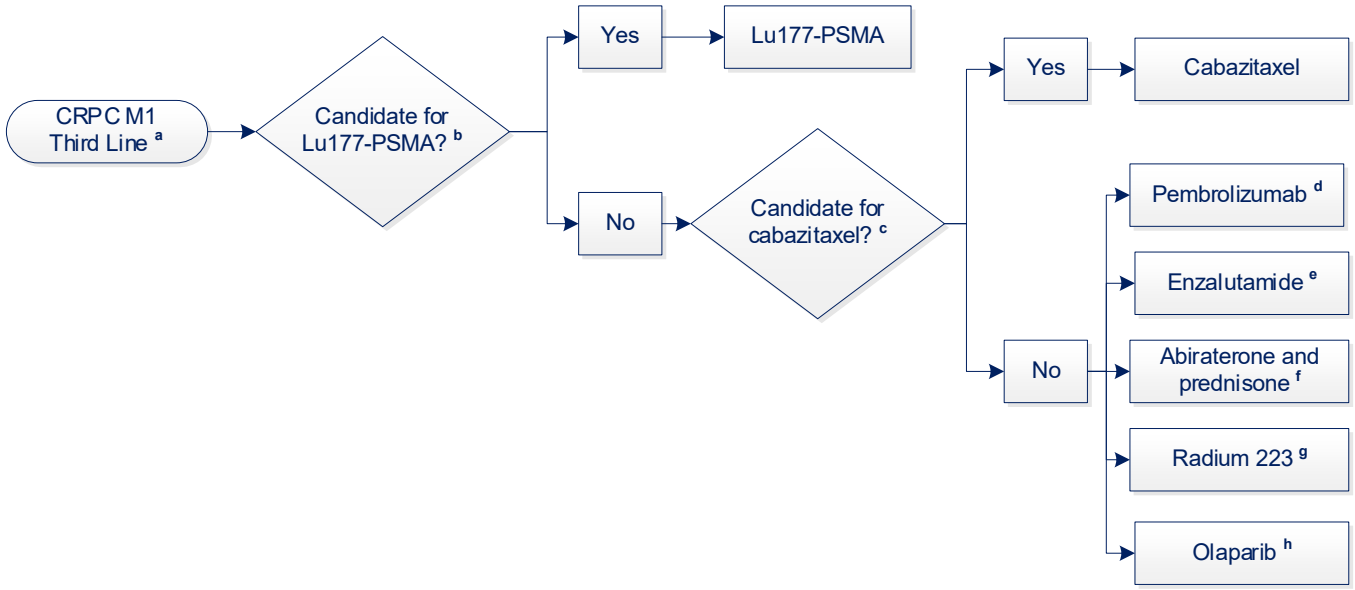
[e] **Abiraterone** prescribe if not previously received (response unlikely if previously progressed on enzalutamide or other androgen receptor antagonist); contraindications include hepatic dysfunction, significant cardiovascular disease, uncontrolled hypertension, or the inability to tolerate prednisone

[f] **Cabazitaxel** favored for use after previous failure of one ART (enzalutamide/abiraterone); avoid repeat of previously used therapies

[g] **Radium 223** prescribe if patient has symptomatic bone metastases and no visceral disease

[h] **Olaparib** prescribe if not previously received and patient has HRRm (Homologous Recombination Repair mutation)

Prostate Cancer – Castrate Resistant Prostate Cancer (CRPC) M1, Third Line



Clinical trial(s) always considered on pathway.

[a] **Consider biopsy** in setting of visceral disease or atypical progression (scan worsening without overt PSA progression); continuous ADT with testosterone goal <50

[b] **Lu177-PSMA** contraindications cannot be given with radium 223, cabazitaxel, or investigational product; patient can continue standard care i.e., AR-directed therapy

[c] **Cabazitaxel** favored for use after previous failure of one ART (enzalutamide/abiraterone); avoid repeat of previously used therapies

[d] **Pembrolizumab** prescribe if patient has MSI-H (microsatellite instability-high), dMMR (deficient mismatch repair) or TMB high in tumor agnostic fashion

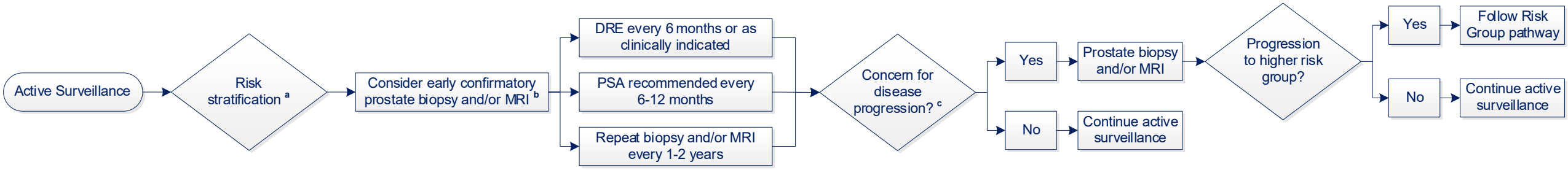
[e] **Enzalutamide** prescribe if not previously received (response unlikely if previously progressed on abiraterone);contraindications include severe renal impairment (CcCl <30 ml/min), seizure history, and/or brain metastases/active epidural disease

[f] **Abiraterone** prescribe if not previously received (response unlikely if previously progressed on enzalutamide or other androgen receptor antagonist); contraindications include hepatic dysfunction, significant cardiovascular disease, uncontrolled hypertension, or the inability to tolerate prednisone

[g] **Radium 223** prescribe if patient has symptomatic bone metastases and no visceral disease

[h] **Olaparib** prescribe if not previously received and patient has HRRm (Homologous Recombination Repair mutation)

Prostate Cancer – Active Surveillance



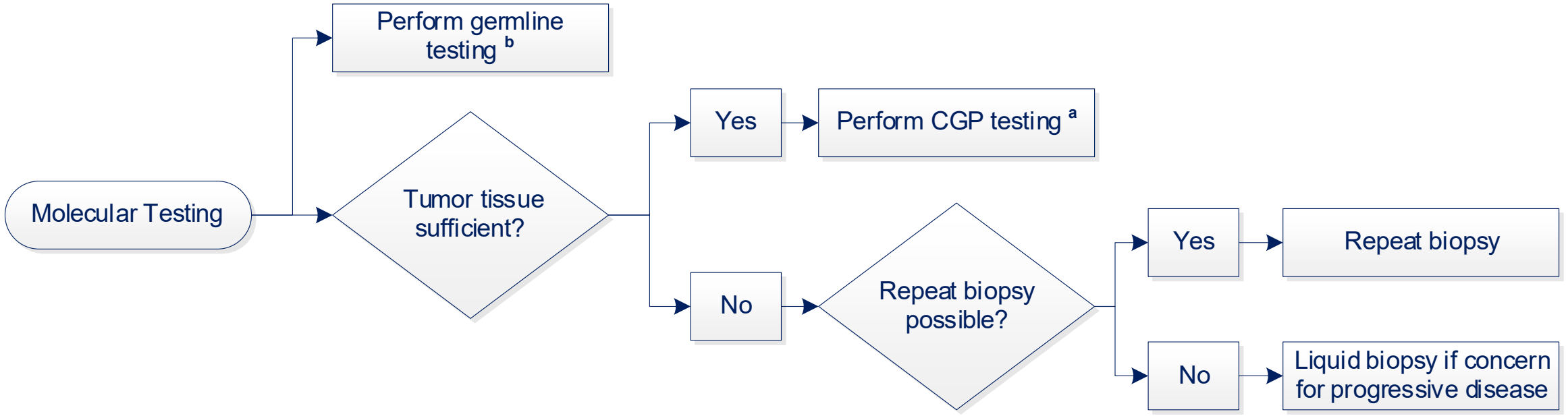
Clinical trial(s) always considered on pathway.

[a] **Risk Stratification** based on a combination of factors that would impact the likelihood of clinically relevant disease progression including: life expectancy (reassess every 1-2 years; if limited life expectancy consider observation), risk group, PSA velocity, DRE, MRI findings, clinical concordance, and patient preference

[b] **Confirmatory Prostate Biopsy** consider if there is a discordance between pathologic and clinical findings or if initial biopsy is determined to be inadequate

[c] **Concern for Disease Progression** based on DRE, PSA, and/or MRI results

Prostate Cancer – Molecular Testing



[a] **CGP Testing** for metastatic disease

[b] **Germline Testing** for high risk, very high risk, regional risk, and metastatic disease

CGP Comprehensive Genomic Profiling

Prostate Cancer – Molecular Testing Table

Eligibility	Test Category	Test Type
Very low, low, or intermediate risk prostate cancer with: 1.) Ashkenazi Jewish ancestry (non-metastatic, T1 or T2), 2.) family history of high-risk germline mutations (non-metastatic, T1 or T2), or 3.) strong family history of cancer (non-metastatic, T1 or T2)	Germline NGS*	Germline prostate cancer panel or common hereditary panel (**POC) or referral to CCGS
High risk or very high risk prostate cancer (non-metastatic, T3 or T4)	Germline NGS*	Germline prostate cancer panel or common hereditary panel (**POC) or referral to CCGS
Regional risk prostate cancer (any T, N1) non-metastatic	Germline NGS*	Germline prostate cancer panel or common hereditary panel (**POC) or referral to CCGS
	Somatic NGS	CGP (Solid); CGP Liquid if tissue insufficient/NA
	IHC	MLH1, MSH2, MSH6, PMS2
Metastatic prostate cancer (any T, any N, M1)	Germline NGS*	Germline prostate cancer panel or common hereditary panel (**POC) or referral to CCGS
	Somatic NGS	CGP (Solid); CGP Liquid if tissue insufficient/NA
	IHC	MLH1, MSH2, MSH6, PMS2
*Germline NGS test should include BRCA1/2, ATM, CHEK2, HOXB13, MLH1, MSH2, MSH6, PMS2, NBN, TP53		
** POC: Point of Care (Provider orders Germline genetic test)		

Questions?

Contact VHAOncologyPathways@va.gov